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EXAMINER	
FREDMAN, JEFFREY NORMAN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,399	NERN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 26, 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14 and 66-70* is/are pending in the application.

4a) Of the above claim(s) *69 and 70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14 and 66-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Claims 69 and 70 are drawn to Group I in the original restriction. Therefore, the original election, on June 2, 2003, elected Group III. So these claims are non-elected and will not be examined. (As a separate point, these appear to be reach through claims and would not satisfy 112, first paragraph in any case).

Claim Rejections - 35 USC § 112 – Use claim

2. The rejection of claims 11-13 under 35 U.S.C. 101 is moot in view of the cancellation of these claims.

Claim Rejections - 35 USC § 112 – Written Description

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 14 and 66-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed

by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

Claims 14 and 66 are drawn to contacting agents with nucleic acids or proteins expressed from those nucleic acids where there is 95% homology with SEQ ID NO: 1 in the presence of any Gbeta protein that associates with Cdc24p or homologues thereof. Claims 67 and 68 are more limited to SEQ ID NO: 1 or a region of SEQ ID NO: 23. All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The claimed genus expressly includes homologues for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID No 1 and 23. Thus, applicant has express possession of only two particular CDC24 nucleic acids, in a genus which comprises hundreds of millions of different possibilities.

It is important to note that there are no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and expressly claim all homologue. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the "homologue" or "95%" sequences of SEQ ID NO: 1 or 23 lack any specific structure. This is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the two sequences, is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim to "95%" or to a "homologue" of SEQ ID NO: 1 or 23, for example.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a deletion, without any definition of the particular 95% variations or homologues claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise 95% variants or homologues of SEQ ID NO: 1 and 23. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 112 - Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 14 and 66-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for screening SEQ ID Nos: 1 and 23, does not reasonably provide enablement for "95%" or homologues of SEQ ID NOs: 1 and 23 as well as any "Gbeta that is capable of interacting with Cdc24p or any homologue thereof". The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method of screening for agents which affect the interaction of cdc24 with a GB or Rho GTPase. The invention is in an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass not only screening for agents which affect the interaction of cdc24 with a GB or Rho GTPase where cdc24 comprises SEQ ID NO:s 1 or 23 but also comprises screening using homologues of SEQ ID NOs: 1 and 23. Further, not only is the specific target not well defined, but the Gbeta is also note well defined, since it represents any homologue of Cdc24p. The method broadly

encompasses the use of the method in any cell type, using any alteration of the proteins, with any mutation whatsoever.

Quantity of Experimentation

The quantity of experimentation in this area is immense since there is significant variability in the homologues of SEQ ID NOs: 1 and 23. This variability is further impacted by the cellular environment and by the significant variability in the effect of receptors, since each receptor is often exquisitely sensitive to different molecules. Therefore, screening the homologues of SEQ ID NOs: 1 and 23 is an inventive, unpredictable and difficult undertaking in itself, beyond the invention of simply screening SEQ ID NO: 1 and 23 themselves. This further effort would require years of inventive effort, with each of the many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art teaches that proteins that are very similar in sequence can have very different function. For example, Rost (J. Mol. Biol. (2002) 318:595-608) notes "The results illustrated how difficult it is to assess the conservation of protein function and to guarantee error free genome annotations, in general, sets with millions of pair comparisons might not suffice to arrive at statistically significant conclusions (see abstract)". Thus, Rost shows that sequence information is insufficient and unpredictable with regard to protein function. However, even if the proteins are of known sequence and known to be highly related to one another, there can still be significant differences in their function. For example, Han et al (Biochem. J. (2001) 355:417-423) teaches regarding a pair of proteins with almost 80% similarity (see page

418, column 2) that "The different tissue expression patterns and regulation during embryonic development suggest that the CEACAM1 and CEACAM2 proteins, although highly similar, may have different functions both during mouse development and in adulthood (see abstract)." Here, there is no requirement in the current claims that the proteins even share any significant homology and the prior art shows that even where there is 80% homology, it is unpredictable to assume that there is similar function because these two proteins have different functions. This point is bolstered by Jin et al (Plant Mol. Biol. (1999) 41:577-585) who notes "Although functional similarities exist between R2R3 MYB proteins that are closely related structurally, there are significant differences in the ways very similar proteins function in different species and also within the same organism. Therefore, despite the large number of R2R3 MYB proteins in plants, it is unlikely that many are precisely redundant in their functions (see abstract)." Thus, there is significant unpredictability regarding the functional relationship of proteins even among structurally related proteins, demonstrating the extreme unpredictability involved in claims broadly drawn to homologues of SEQ ID NOs: 1 and 23.

Working Examples

The specification has a working example using SEQ ID Nos 1 and 23.

Guidance in the Specification.

The specification, while teaching SEQ ID NO: 1 and SEQ ID NO: 23, does not teach the structure or function of derivatives, fragments, variants or homologues of these sequences. In particular, the specification lacks any discussion or guidance towards specific domains, specific conserved amino acids or specific regions within the sequences which are absolutely required for protein function. The specification also

lacks any guidance with regard to limitations on homologues to guide in selection from the literally many hundreds of billions of different possible genus members.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the presence of a working example which does not address the scope of the claim and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

7. The rejection of claims 11-16 under 35 U.S.C. 102(b) is withdrawn in view of the amendment.

Response to Arguments

8. Applicant's arguments filed January 26, 2004 have been fully considered but they are not persuasive.

Applicant indicates that the examiner agreed that the claims would be allowable in an interview. The examiner believes that the claims are in better form, but if the impression was given that the amendment was certain to result in allowance, the

impression is regretted and is not correct. The claims still fail to meet the written description and enablement requirements for the reasons given in those rejections.

Applicant argues that the use of 95% alone is sufficient to overcome the written description rejections. This is not correct because in situations where 95% is found to be sufficiently described, the compound at issue has a specific enzymatic function which is recited in the claim. In this case, no such function is evident. The function is the ability to interact with the agent "in the presence of a Gbeta capable of being associated with Cdc24p or a homologue thereof". So this function is entirely undefined and does not impose any structural constraints on the molecule. That is, unlike in the situation where a specific enzyme is recited, here there is significant variability permitted by the interaction and therefore the claims do not meet the written description requirement.

Even for the new claims 67 and 68, in which SEQ ID NO: 1 is defined, the homologue language leaves the claims open since there is significant variability which is not defined or possessed that may be presented in these homologues. This is most clearly demonstrated in claim 67 where the claim reads on "an expression product of the homologue of the nucleotide sequence shown as SEQ ID NO: 1." What is this? This might be a protein that is encoded in part by SEQ ID NO: 23, but this expression product is not described by the specification in such a way as to put in possession of the reader of this specification.

Similarly, the enablement rejection is not overcome because there is still significant unpredictability in which molecules are being screened, and the results are

particularly unpredictable due to the variation in the Gbeta's permitted, since any Gbeta which will interact with Cdc24p or any "homologue" thereof, which potentially reads on a huge number of proteins, most of which are not currently known.

Therefore, the written description and enablement rejections are maintained.

The 102 rejection is withdrawn in view of the amendment.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
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Art Unit 1634